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EDITORIAL COMMENT

CT Angiography for All Patients With Inconclusive Noninvasive Test? Clinical Perspective: "Not Yet"*

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It has been known since the early 1970s that the extent and severity of coronary artery disease (CAD) is a predictor of outcomes (1). Multidetector coronary computed tomography (MD-CCT) is a useful diagnostic test in the assessment of CAD (2). Although it is a minimally invasive test, MD-CCT carries attendant risks. There is a risk for development of contrast-induced nephropathy (CIN), which is significantly higher with intravenous contrast as compared with intra-arterial contrast (3). CIN is associated with an increased mortality of 15.6% at 30 days with an odds ratio (OR) of 3.37 (95% confidence interval [CI]: 2.58 to 4.41; $p < 0.001$) (3). Current MD-CCT protocols use a radiation dose similar to that of nuclear myocardial perfusion and approximately twice that of invasive coronary angiography (ICA) (4). The assessment by MD-CCT of lesion stenosis in phantom models is comparable to ICA (5); however, coronary revascularization, either surgical or percutaneous, is usually not performed without prior ICA. Ideally, MD-CCT should be performed in circumstances in which the information provided would obviate the need for ICA and in whom further radiation and contrast exposures would be limited to therapeutic procedures.

See page 740

In this issue of *iJACC*, Azevedo et al. (6) showed the presence of CAD on MD-CCT provided independent prognostic information about subsequent death and nonfatal myocardial infarction in a select cohort of 529 patients who had inconclusive noninvasive cardiac stress tests. The presence of increasing extent and severity of coronary artery obstruction diagnosed by MD-CCT was associated with an increase in the *combined* endpoint of death and nonfatal myocardial infarction. The hazard ratio of the combined endpoint using multivariate analysis was 3.15 (95% CI: 1.26 to 7.89) in patients with ≥50% stenosis in any coronary artery when adjusted for coronary calcium score, age, and diabetes. Increasing degrees of disease, when scored by the Duke CAD Index, were also associated with increased risk when adjusted for the same clinical variables. Multivariate analysis did not include adjustment for the presence of smoking, dyslipidemia, and hypertension.

However, there are concerns regarding the applicability of these findings to routine clinical practice. These relate to:

1. **Patient population**. Information regarding the indications for the initial stress testing was not provided. This test was performed in patients at very low risk, for example, 1 patient was 22 years old. At the other extreme, 42 patients had typical angina; the mean age of the patients in this study was 57.8 years, and 61% of the population were men. In men of this age with typical angina, the pretest probability of significant CAD is 93% (7), and thus noninvasive testing is likely to be of questionable additional value. The guidelines deem patients with high- or low-risk features on exercise treadmill testing inappropriate for MD-CCT (8). MD-CCT is recommended in patients with intermediate risk on exercise treadmill testing, have equivocal results after noninvasive imaging, or have discordant results of exercise treadmill testing and noninvasive imaging (8). In this study, patients with high or low risk were included in the initial noninvasive tests and for MD-CCT.

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2. **Treatment of comorbid conditions**. Ford et al. (9) demonstrated that the treatment of CAD risk factors has contributed more to the reductions in cardiovascular mortality than cardiac-specific treatments. Appropriate and timely treatment of comorbid conditions such as diabetes mellitus, hypertension, and dyslipidemia together with appropriate antianginal medications can be expected to improve patient outcomes in patients with stable angina (10,11). The authors state that treatment of patients followed "actual clinical practice," however, information regarding patient treatments and whether treatment goals were met was not provided. Thus, it is uncertain whether the increased events in patients with high-risk MD-CCT findings were due solely to differences in CAD burden or to differences in treatment as well. Data on CIN were also not provided.
3. **Patient outcomes**. The causes of death were not described, and it is not known how many patients died of cardiovascular disease; the predictors of death were also not presented. The risk-adjusted hazard ratio for those with severe stenosis was 13.29 (95% CI: 2.47 to 71.32). The event rate in the 104 patients with severe stenosis who had ≥70% obstruction of CAD was not provided. It is also not known whether the findings on MD-CCT altered the management and treatment of the patients. Knowing that death was not likely related to cardiovascular disease would be helpful in assuring that treatment that ensued after MD-CCT may have been beneficial. Sixty-eight patients underwent revascularization; did these patients have ICA prior to the procedure? The ICA would have added to further radiation and contrast exposure. It is prudent to be judicious in the use of tests that cause significant radiation exposure. Radiation dosage is lower in currently available MD-CCT.

The authors presented prognostic data that are interesting and useful (6). The study group was "homogenous," and partly by design, was aligned with current appropriateness guidelines. However, given the considerations outlined in the preceding text, there are limitations to this study. The authors provided no information that the findings on MD-CCT in patients with appropriate indications for noninvasive testing and with appropriate, but inconclusive, tests resulted in any benefit to patient care by improving treatment(s) and quality of life and/or by reducing the incidence of subsequent myocardial infarction or deaths from cardiovascular causes. Future studies need to be more focused and should document whether better outcomes occur because of the result(s) of the test. At that time, the risks of the procedure should be balanced against the benefits.

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